Anthrax

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Key features

- Anthrax is an acute bacterial zoonosis predominantly of herbivorous animals
- It is caused by *Bacillus anthracis* that persists in the environment as dormant spores and may be transmitted to humans by inoculation, inhalation, or ingestion
- The majority of naturally occurring human cases involve the skin; only very rarely are the respiratory and gastrointestinal tracts affected
- Cutaneous anthrax is characterized by the development of a papule followed by a black eschar, often surrounded by significant edema. It may be complicated by septicemia and death in 5–20% of untreated cases
- Inhalational anthrax and gastrointestinal anthrax, both characterized by regional lymphadenitis and septicemia, have a mortality rate approaching 100% if untreated and ~50% even with antimicrobial therapy and supportive care
- Vaccines are available

Abstract

Anthrax is an acute bacterial zoonotic disease of herbivorous animals caused by *Bacillus anthracis*, a Gram-positive toxinogenic encapsulated spore forming bacillus. Under natural conditions, humans become infected by inoculation or more rarely ingestion or inhalation of organisms from infected animals or contaminated animal products. The disease occurs world-wide and is endemic in grazing animals in less developed countries. It occurs very rarely in developed countries but the use of anthrax spores to intentionally cause human disease has

heightened awareness of the disease. If recognized early, cutaneous anthrax is readily treatable with antibiotics. Inhalational and gastrointestinal anthrax are associated with high mortality of ~50% even with appropriate antibiotics and modern supportive care. Exposure to an aerosol of spores is best managed by the combination of a prolonged course of antibiotics and vaccination.

Introduction

Anthrax is an acute bacterial zoonosis, predominantly of herbivores, caused by *Bacillus anthracis*. Animal anthrax is rare in developed nations as a result of intensive surveillance and control. However, the disease remains endemic in animals and not uncommon in humans in many developing countries. Humans become infected after contact with infected animals or contaminated animal products by inoculation, ingestion, or inhalation. A major concern is the use of anthrax to intentionally cause disease, as occurred in 2001 with the mailing of letters containing anthrax spores.

Epidemiology

Incidence of Human Anthrax

Human infection with *B. anthracis* is infrequent in developed countries. Approximately 20,000–100,000 cases of human anthrax are estimated to occur annually worldwide, although accurate figures are impossible to obtain. However, anthrax is ubiquitous in agricultural nations dependent on animal husbandry. Epidemics of human anthrax are rare. Large outbreaks of cutaneous anthrax occurred during wars in Zimbabwe in 1978–1980 and in Chad in 1988. The largest epidemic of inhalational anthrax occurred in 1979 in Sverdlovsk (Ekaterinburg), Russia resulting from the accidental release of spores from a military facility. In 2001, 22 cases of bioterrorism-related anthrax (11 inhalational) occurred after envelopes containing spores were mailed through the United States Postal Service.

Zoonotic Anthrax

Anthrax is chiefly a disease of herbivores. Animals are infected via the gastrointestinal tract by grazing on contaminated pasture and rarely by contact with other infected animals. Before death, animals often contaminate the soil with infected saliva, blood, urine, or feces. Soil, forage and, to a lesser extent, groundwater are major reservoirs of anthrax.

Geographic Occurrence

Outbreaks are sporadic in developed nations, while disease remains endemic in parts of Africa, India, Southeast Asia, the Middle East, Greece, Albania, southern Italy, Romania, the former Soviet Union, and Central and South America (Fig. 1). *Bacillus anthracis* spores germinate in soil at 20–44°C in areas with **>**85% humidity. Germinated bacilli are destroyed by other soil microbes. Therefore, in many tropical regions, animal anthrax occurs predominantly in the dry season, with some persistence into the wet season. It is likely that persistence in soil results from amplification caused by growth in infected animals and sporulation in animal carcasses with subsequent contamination of the soil. Vultures and non-biting flies may be responsible for dissemination of anthrax.

Human Anthrax

Human anthrax is traced to agricultural, industrial or, rarely, laboratory acquisition. Only two cases of human-to-human transmission have been reported involving contact with a cutaneous case.

Industrially Acquired Anthrax

In economically developed countries, industrial acquisition accounts for ~80% of cutaneous anthrax and almost all inhalational anthrax, and occurs predominantly among tanners or leather, hair, wool, or bone-meal fertilizer workers. Subclinical infection and seroconversion among

workers in these industries may be more common than overt illness. Infections in developed countries are acquired from contaminated animal hides, hair, or bones imported from developing countries with zoonotic anthrax. Leather goods and drums from Haiti and West Africa have been vehicles of anthrax transmission. Recently, cutaneous cases have been seen in heroin addicts in four European countries.

Agricultural Anthrax

In developed countries, contact with infected animals by farmers, butchers, and veterinarians is implicated in ~20% of cutaneous cases. Transmission by biting insects has been suspected and bone-meal fertilizer implicated in sporadic cases of inhalational anthrax among gardeners.

Natural History, Pathogenesis, and Pathology

Anthrax bacilli are large (1.0–1.5 μm by 3–8 μm), non-motile, Gram-positive rods. Abundant in smears of blood and tissues, bacilli occur singly or in short chains. *Bacillus anthracis* also develops spores in culture or soil, but not *in vivo* unless exposed to ambient air. Spores are resistant to heat and many disinfectants. They are destroyed by boiling for 10 min, dry heat (140°C) for 3 h or autoclaving (121°C) for 15 min, but remain viable for years in dry soil. Cattle have become infected by grazing in fields where animals died of anthrax decades before [1].

***Bacillus anthracis* Virulence Factors**

Bacillus anthracis possesses three major virulence factors: a poly-γ-D-glutamic acid capsule and two protein exotoxins. The capsule is antiphagocytic, enabling the bacillus to resist killing by leukocytes. The anthrax toxins are composed of a eukaryotic cell receptor-binding protein and a second protein possessing cytotoxic activity. The cell receptor-binding protein protective antigen combines with edema factor, a calmodulin-dependent adenylate cyclase, to produce edema toxin or with lethal factor, a zinc metalloprotease, to produce a lethal toxin. Protective antigen is

necessary for binding and translocation of the cytotoxic proteins. Edema toxin raises intracelluar levels of cyclic adenosine monophosphate (cAMP), interfering with cell function, while lethal factor inactivates mitogen-activated protein (MAP) kinases, interfering with signal transduction [2]. The toxins interfere with innate immunity, having been shown *in vitro* to impair the function of neutrophils, macrophages, lymphocytes, and dendritic cells [3]. Additional effects of toxins occur *in vivo* because toxin receptors are expressed on many cells, including those of the cardiovascular system and liver [4].

Cutaneous Anthrax

Cutaneous anthrax follows inoculation of spores into skin. Spores then germinate and the bacilli multiply and elaborate their virulence factors. Hematogenous dissemination follows in 5–20% of untreated cases. Cutaneous lesions may demonstrate satellite bullous lesions in which Gram-positive bacilli can be observed; pus is not present.

Inhalational Anthrax

Inhalational anthrax follows the inhalation of spores of 1–5 μm in diameter. Larger particles are cleared by the mucociliary mechanism of the lungs. Spore aerosols may be encountered by workers handling contaminated batches of hair, wool, or bone-meal fertilizer. The aerosol infective dose for human infection is high – in wool mills, non-immune workers inhaled as many as 510 spores of 5 μm or less in diameter per 8-hour shift without becoming ill. Animal studies indicate that inhaled spores are ingested by alveolar phagocytes and carried to tracheobronchial and mediastinal lymph nodes. There, the spores germinate into bacilli with the production of capsule and toxins. Hemorrhagic edema and necrosis of mediastinal lymph nodes ensue. Alveoli show a hemorrhagic exudate and only rarely bacilli; neutrophils are usually absent. Alveolar

capillaries contain fibrin thrombi and bacilli [5]. Hemorrhagic pleural effusions commonly occur. Hematogenous dissemination to the meninges, spleen, and intestine can occur.

Gastrointestinal Anthrax

Oropharyngeal and intestinal anthrax follow ingestion of poorly cooked, contaminated meat [6]. An ulcer in the stomach, terminal ileum, or cecum may be present, and hemorrhage and edema of regional lymphatics occurs.

Septicemic Anthrax

Generalized sepsis may follow cutaneous anthrax and, almost invariably, accompanies inhalational and gastrointestinal anthrax. Vascular injury may result from the proliferation of bacteria in the blood and effects of the exotoxins acting directly on the endothelium or indirectly through other mediators. Widespread capillary thrombosis, circulatory failure, and shock occur prior to death. Adrenocortical hemorrhage can occur. In addition, anthrax bacteremia may lead to hemorrhagic meningitis. The leptomeninges reveal scant inflammation but widespread hemorrhages. The brain has hemorrhages and generalized cerebral edema. Subarachnoid hemorrhage may also occur.

Clinical Features

Cutaneous Anthrax

Cutaneous anthrax accounts for **>**95% of human infections and commonly involves areas of the face, neck, hands, and arms [7]. The incubation period is 12 hours to 7 (mean 3) days. The initial lesion is a small, erythematous macule or papule. It turns brown and develops a ring of erythema and a vesicle. Vesicular satellite lesions may appear (Fig. 2) and, after a few days, the clear, vesicular fluid becomes blue-black from hemorrhage. The papule ulcerates, developing a black eschar by the fifth to seventh day. Non-pitting, gelatinous edema may be prominent, occasionally

extending to the iliac crest from lesions of the head and neck. This so-called “malignant edema”, together with a black eschar, is pathognomonic for anthrax. Patients have few symptoms, most commonly malaise, headache, and low-grade fever.

Inhalational Anthrax

Inhalational anthrax accounts for **<**5% of reported cases. Nonspecific symptoms of mild fever, malaise, fatigue, and myalgia develop 1–5 days after exposure; nonproductive cough is often reported. In cases occurring in the 2001 epidemic, nausea or vomiting was common [8] and some had extreme fatigue and severe headache. Patients may have transient improvement after several days or may directly develop severe respiratory distress with cyanosis, diaphoresis, increased fever, and tachycardia. Stridor, diffuse rales, and basilar dullness may be heard. Chest radiographs reveal symmetric, characteristic mediastinal widening, pleural effusions and, in some cases, patchy infiltrates (Fig. 3). Massive, superficial edema of the head and neck may occur. Meningitis, often hemorrhagic, occurs in ~50% of cases. Pleural effusions may also be hemorrhagic. *Bacillus anthracis* is usually isolated in cultures of blood, pleural fluid, and cerebrospinal fluid.

Gastrointestinal Anthrax

Oropharyngeal and gastrointestinal anthrax account for **<**5% of cases. Oropharyngeal anthrax presents with sore throat, an ulcer in the oral cavity, dysphagia, cervical and submandibular lymphadenopathy, and often dramatic neck edema. Gastrointestinal anthrax develops after an incubation period of 2–5 days. Patients have generalized abdominal pain, anorexia, nausea, vomiting and, in some cases, hematemesis. Severe prostration accompanies the development of

ascites, bloody diarrhea, toxemia, and shock. Subcutaneous edema may extensively involve the lower trunk.

Central Nervous System (CNS) Anthrax

Anthrax meningitis follows bacteremia from a cutaneous, pulmonary or intestinal source. Patients usually present with fever, meningismus, and rapidly deteriorating mental status. Lumbar puncture reveals spinal fluid containing Gram-positive rods and is often hemorrhagic. Bacteremia occurs in 70% of patients; the usual survival is 2–4 days. In very rare cases, patients present with isolated meningitis without other evidence of disease.

Patient Evaluation, Diagnosis, and Differential Diagnosis

Differential Diagnosis

The epidemiologic background of an industrial or agricultural exposure, the evolution of a pruritic then painless lesion without cellulitis or lymphangitis, and the dramatic appearance of the black eschar and extensive non-pitting edema help to distinguish anthrax from other skin infections. The initial, nonspecific symptoms of inhalational anthrax may resemble influenza, bronchitis, or the common cold; however, there are no upper respiratory symptoms in inhalational anthrax [9]. The later stage may mimic congestive cardiac failure but should be suggested by mediastinal widening on chest radiographs in the setting of occupational exposure. Anthrax meningitis may be confused with other forms of bacterial meningitis or subarachnoid hemorrhage. Intestinal anthrax with fever and severe abdominal pain will only be recognized pre-surgery or premortem if the appropriate epidemiologic history is obtained.

Direct Smear and Culture Diagnosis

In cutaneous anthrax, encapsulated bacilli can be identified on Gram- or Giemsa-stained smears and readily cultured. Bacilli may also be abundant in cerebrospinal or pleural fluid in cases of

inhalational anthrax. Direct fluorescent antibody stains for cell wall and capsule are available for definitive, early identification of *B. anthracis* from vesicular fluid, tissue or culture. On sheep blood agar, 3- to 5-mm, gray-white, opaque, rough, non-hemolytic colonies become evident within 24 h. In the presence of carbon dioxide, the organism produces a capsule and the colony is round and mucoid. Identification is confirmed immunologically by the presence of the capsule, susceptibility to specific bacteriophage and testing by PCR for toxin and capsule genes.

Serologic Diagnosis

Antibody to protective antigen or capsule, measured by ELISA, develops in 67–94% of cases of cutaneous or oropharyngeal anthrax and in 100% of inhalational anthrax cases, but is only useful retrospectively. Rapid diagnostic tests for the detection of protective antigen, lethal factor, and capsule in body fluids have been developed and shown to be of value in nonhuman primate models and one human case.

Treatment

Consensus treatment recommendations for both adults and children are available and have recently been updated [10-11].

Cutaneous Anthrax

Untreated cutaneous anthrax can progress to septicemia, shock, renal failure and, in 5–20% of cases, death. Almost all cutaneous cases are cured with effective antimicrobial therapy. Treatment with an oral fluoroquinolone (ciprofloxacin, levofloxacin or moxifloxacin) or doxycycline for 7–10 days is recommended by the United States Centers for Disease Control and Prevention (CDC) for uncomplicated cases of naturally acquired cutaneous anthrax [10], although a study conducted in Turkey suggests that antibiotic treatment for 3–5 days is as effective as 7–10 days. Clindamycin is an alternative option if fluoroquinolones or doxycycline

is unavailable or contraindicated. Oral therapy with amoxicillin or penicillin VK can be used for penicillin-sensitive isolates. For cutaneous anthrax associated with a bioterrorism attack, the duration of treatment is 60 days, due to potential exposure to airborne spores. Amoxicillin can be used to complete the 60-day course for penicillin-sensitive isolates. Recommended antibiotics and doses for both adults and children for the treatment of cutaneous anthrax are shown in Table 1 [10,11]. Treatment for severe cutaneous anthrax with bacteremia is the same as for inhalational and gastrointestinal anthrax, which require intravenous antibiotics as described below.

Other Anthrax Syndromes

Historically, the treatment for systemic anthrax which includes cutaneous anthrax with bacteremia, inhalational and gastrointestinal anthrax was high-dose intravenous penicillin. However, the recently updated CDC anthrax treatment guidelines, based on experience derived from the 2001 cases, recommend a multi-drug regimen of intravenous [IV] antibiotics for systemic anthrax [10,11]. The specific antibiotics recommended are based on whether meningitis is suspected, confirmed or ruled out. If meningitis has not been ruled out, the guidelines recommend three or more antimicrobial drugs with activity against *B. anthracis*, including a fluoroquinolone, a ß-lactam and a protein synthesis inhibitor. All the antimicrobial agents should have good CNS penetration. The duration of IV antibiotic treatment is for $\geq$2 weeks or until the patient is clinically stable, whichever is longer. The treatment of systemic anthrax where meningitis has been ruled out is similar to the treatment with meningitis, with the following exceptions. First two or more antimicrobial drugs should be used. At least one of these should have bactericidal activity and at least one should be a protein synthesis inhibitor. If the *B. anthracis* infecting strain is susceptible to penicillin, then penicillin G is considered to be equivalent to the fluoroquinolones as the bactericidal agent. Finally, antimicrobial drug

penetration into the CNS is not as important. Recommended antibiotics and doses for the treatment of systemic anthrax, with and without suspected meningitis, for both adults and children are given in Table 1 [10,11]. To complete a 60-day course of therapy, treatment can be switched to oral medicines when the patient is stable. There are no controlled studies for human inhalational anthrax to determine the optimal duration of treatment and if a shorter period is adequate– the suggested 60-day course of antibiotics is based on the possible germination of retained dormant spores late after infection. Although historically viewed as invariably fatal, data from the 2001 inhalational anthrax cases showed that a multidrug antibiotic regimen combined with supportive therapy reduced mortality to 45% [12].

Antitoxin

The use of an antitoxin in conjunction with antimicrobial therapy is recommended for the treatment of systemic anthrax although there are no controlled clinical studies demonstrating its added benefit. There are three antitoxins in the CDC Strategic National Stockpile: Raxibacumab (GlaxoSmithKline, London UK), Anthrax Immune globulin Intravenous (AIGIV) (Emergent BioSolutions, Gaithersburg, MD, USA) and Obiltoxaximab (Elusys Therapeutics Inc, Pine Brook, NJ, USA).

Supportive Therapy

The evolution of the anthrax skin lesion is not modified by antimicrobial treatment. Pleural fluid drainage was likely associated with decreased mortality in the 2001 anthrax cases, by reducing toxin levels and decreasing lung compression. Although data in anthrax is lacking, adjunctive intravenous dexamethasone is recommended in addition to antimicrobial therapy for patients suspected of having meningitis.

Isolation of Patients

Human-to-human transmission has not been observed in inhalational or gastrointestinal anthrax. Therefore, standard infection control precautions should suffice. However, if bloody sputum is present, respiratory isolation should be instituted. Because of the potential infectious nature of an untreated cutaneous anthrax lesion or gastrointestinal anthrax, contact and secretion precautions should be used.

Post-exposure Prophylaxis (PEP)

PEP requires a different therapeutic approach compared with treatment of established disease. Most spores deposited into the alveolar spaces germinate within a few days. However, germination is not synchronous. Studies have demonstrated viable spores in the lungs of rhesus macaques 100 days after exposure and anthrax has occurred several months after exposure in animals given antibiotics for short periods. As spores can remain dormant for long periods and antibiotics act only after spores have germinated, PEP to prevent disease from dormant spores that may subsequently germinate requires either a prolonged course of antibiotics or antibiotics plus vaccination. The current CDC recommendation for PEP for exposure to aerosolized *B. anthracis* spores is 60 days of oral antibiotics combined with anthrax vaccine (BioThrax) 0.5 ml given subcutaneously at 0, 2 and 4 weeks [13,14]. Antibiotics recommended for PEP include ciprofloxacin or doxycycline. Levofloxacin, moxifloxacin or clindamycin are recommended as a second-line antibiotics. Penicillins should not be used presumptively for PEP of anthrax. However, once the strain is proven to be penicillin-susceptible, amoxicillin or penicillin VK, can be used to complete the 60 day course of therapy. The recommended antibiotics and doses for anthrax post-exposure prophylaxis for both adults and children are listed in Table 2.

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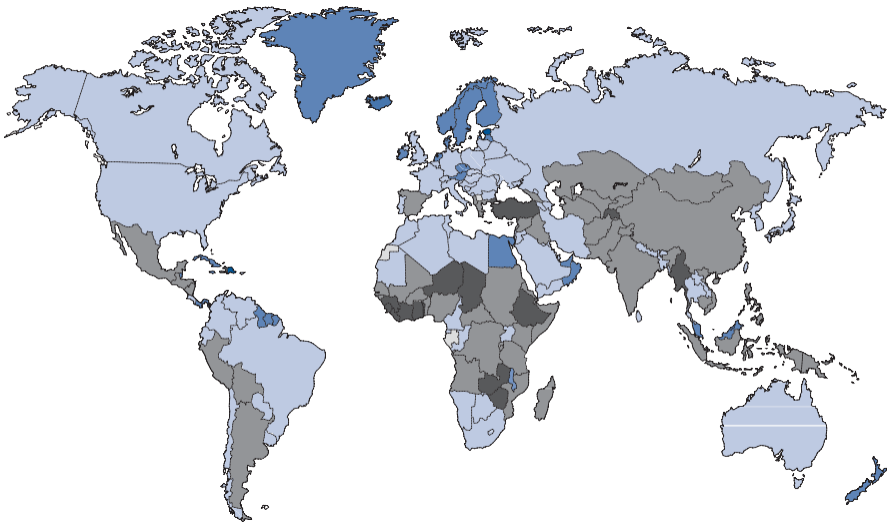
FIGURE 1 Geographic distribution of anthrax (reproduced with permission from World Health Organization, http://www.vetmed.lsu.edu/whocc/mp_world.htm).

FIGURE 2 Cutaneous anthrax in a 45-year-old cattleman. **(A)** Early facial lesion with prominent edema and vesicular satellite lesions that revealed abundant anthrax bacilli on Gram-stain and culture. **(B)** Evolution of the cutaneous eschar despite antimicrobial therapy (courtesy of Dr. Alejandro Morales).

FIGURE 3 Chest x-ray of a case of inhalational anthrax showing mediastinal widening and a small left pleural effusion (reproduced with permission from Jernigan JA, Stephens DS, Ashford DA, et al. Bioterrorism-related inhalational anthrax: the first 10 cases reported in the United States. Emerg Infect Dis 2001;7:933–44.)



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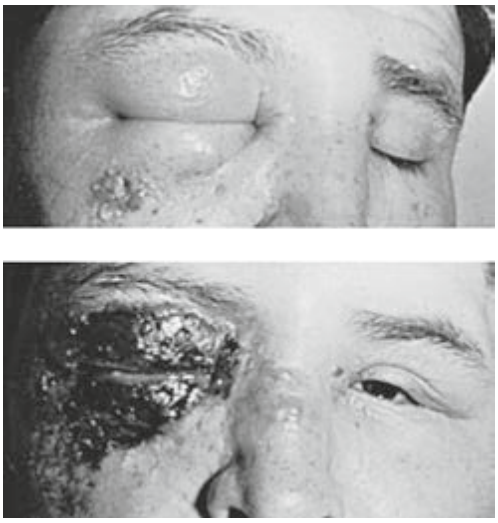
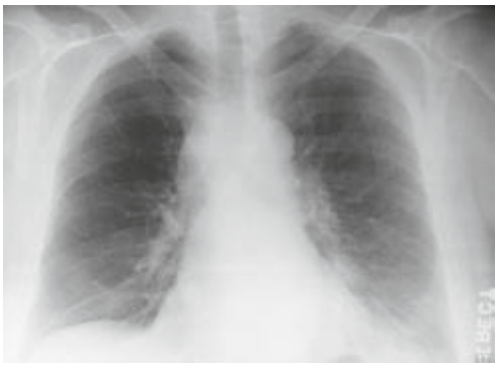


FIGURE 2 Cutaneous anthrax in a 45-year-old cattleman. **(A)** Early facial lesion with prominent edema and vesicular satellite lesions that revealed abundant anthrax bacilli on Gram-stain and culture. **(B)** Evolution of the cutaneous eschar despite antimicrobial therapy *(courtesy of Dr Alejandro Morales).*



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Treatment of Anthrax in Adults and Children

Adults

Cutaneous anthrax	**Systemic anthrax with possible or confirmed meningitis**	**Systemic anthrax when meningitis has been excluded**
Ciprofloxacin 500 mg	**Ciprofloxacin** 400 mg IV q 8 h	**Ciprofloxacin** 400 mg IV q 8 h
PO q 12 h	**or**	**or**
or	Levofloxacin 750 mg IV q 24 h	Levofloxacin 750 mg IV q 24 h
Doxycycline 100 mg	**or**	**or**
PO q 12 h	Moxifloxacin 400 mg IV q 24 h	Moxifloxacin 400 mg IV q 24 h
or	**PLUS**	**or**
Levofloxacin 750 mg	**Meropenem** 2 g IV q 8 h	Meropenem 2 g IV q 8 h
PO q 24 h	**or**	**or**
or	Imipenem 1 g IV q 6 h	Imipenem 1 g IV q 6 h
Moxifloxacin 400 mg	**or**	**or**
PO q 24 h	Doripenem 500 mg IV q 8 h	Doripenem 500 mg IV q 8 h
or	**or**	**or**
Clindamycin 600 mg	Penicillin G[(1)] 4 million units IV q 4 h	Vancomycin 60 mg/kg/d IV divided q 8 h
PO q 8 h	**or**	**or**
or	Ampicillin[(1)] 3 g IV q 6 h	Penicillin G[(1)] 4 million units IV q 4 h
Amoxicillin[(1)] 1 g	**PLUS**	**or**
PO q 8 h	**Linezolid** 600 mg IV q 12 h	Ampicillin[(1)] 3 g IV q 6 h
or	**or**	**PLUS**
Penicillin VK[(1)] 500 mg	Clindamycin 900 mg IV q 8 h	**Clindamycin** 900 mg IV q 8 h
PO q 6 h	**or**	**or**
	Rifampin 600 mg IV q 12 h	**Linezolid** 600 mg IV q 12 h
	or	**or**
	Chloramphenicol 1 g IV q 6 to 8 h	Doxycycline 200 mg IV initially, then 100 mg IV q 12 h
		or

Rifampin 600 mg IV q 12 h

Children

Cutaneous anthrax	**Systemic anthrax with possible or confirmed meningitis**	**Systemic anthrax when meningitis has been excluded**
Ciprofloxacin	**Ciprofloxacin**	**Ciprofloxacin**
30 mg/kg/day PO	30 mg/kg/day IV divided q 8 h	30 mg/kg/day IV divided q 8 h
divided q 12 h	(max 400 mg/dose)	(max 400mg/dose)
(max 500 mg/dose)	**or**	**or**
or	Levofloxacin	Meropenem
Doxycycline	<50 kg: 16 mg/kg/day IV divided	60 mg/kg/day IV divided q 8 h
<45 kg: 4.4 mg/kg/day	q 12 h (max 250mg/dose);	(max 2 g/dose)
PO divided q 12 h	>50 kg: 500 mg IV given q 24 h	**or**
(max 100 mg/dose);	**or**	Levofloxacin
≥45 kg: 100 mg/dose	Moxifloxacin	<50 kg: 20 mg/kg/day IV divided
PO given q 12 h	3 months to <2 years: 12 mg/kg/day IV	q 12 h (max 250 mg/dose);
or	divided q 12 h (max 200 mg/dose);	>50 kg: 500 mg IV given q 24 h
Clindamycin	2-5 years: 10mg/kg/day IV divided q 12	**or**
30 mg/kg/day	h (max 200 mg/dose); 6-11 years:	Imipenem/cilastatin
PO divided q 8 h	8 mg/kg/day IV divided q 12 h	100 mg/kg/day IV divided
(max 600 mg/dose)	(max 200 mg/dose); 12-17 years,	q 6 h (max 1 g/dose)
or	≥45 kg body weight: 400 mg IV q day;	**or**
Levofloxacin[(2)]	12-17 years, <45 kg body weight: 8	Vancomycin
<50 Kg: 16 mg/kg/day	mg/kg/day IV divided q 12 h	60 mg/kg/day IV divided q 8 h
PO divided q12 h	(max 200 mg/dose)	**or**
(max 250 mg/dose);	**PLUS**	**Penicillin G**[(1)]
>50 kg: 500 mg PO	**Meropenem**	400,000 U/kg/day IV divided
given q 24 h	120 mg/kg/day IV divided	q 4 h (max 4 MU/dose)
or	q 8 h (max 2 g/dose)	**or**

Amoxicillin[(1)]

75mg/kg/day

PO divided q 8 h

(max 1 g/dose)

or

Penicillin VK[(1)]

50-75 mg/kg/day PO

divided q 6 to 8 h

or

Imipenem/cilastatin

100 mg/kg/day IV divided

q 6 h (max 1 g/dose)

or

Doripenem

120 mg/kg/day IV divided

q 8 h (max 1 g/dose)

or

Vancomycin

60 mg/kg/day IV divided

q 8 h

or

Penicillin G[(1)]

400,000 U/kg/day IV divided

q 4 h (max 4 MU/dose)

or

Ampicillin[(1)]

400 mg/kg/day IV divided

q 6 h (max 3 g/dose)

PLUS

Linezolid

<12 year old: 30 mg/kg/day IV

divided q 8 h; >12 years old:

30 mg/kg/day IV divided

q 12 h (max 600 mg/dose)

or

Clindamycin

40 mg/kg/day IV divided

Ampicillin[(1)]

200 mg/kg/day IV divided

every 6 h (max 3 g/dose)

PLUS

Clindamycin

40 mg/kg/day IV divided

every 8 h (max 900 mg/dose)

or

Linezolid

<12 year old: 30 mg/kg/day IV divided

q 8 h; >12 years old: 30

mg/kg/day IV divided

q 12 h (max 600 mg/dose)

or

Doxycycline

<45 kg: 4.4 mg/kg/day IV, loading dose

(not to exceed 200 mg); ≥45 kg:

200 mg IV loading dose then,

<45 kg: 4.4 mg/kg/day IV, divided

q 12 h (max 100 mg/dose);

≥45 kg: 100 mg IV given q 12 h

or

Rifampin

20 mg/kg/day IV divided

q 12 h (max 300 mg/dose)

q 8 h (max 900mg/dose)

or

Rifampin

20 mg/kg/day IV divided

q 12 h (max 300 mg/dose)

or

Chloramphenicol

100 mg/kg/day IV divided

q 6 h

(1) for penicillin-susceptible strains

(2) safety data for levofloxacin use greater than 14 days in the pediatric population is limited

Duration of PO therapy for non-systemic cutaneous anthrax is 7-10 days.

Duration of IV therapy of anthrax with possible or confirmed meningitis is ≥2 weeks or until clinically stable whichever is longer.

Duration of IV therapy for anthrax when meningitis has been excluded is ≥2 weeks or until clinically stable whichever is longer.

All patients exposed to aerosolized spores will require prophylaxis to complete an antimicrobial drug course of 60 days from onset of illness.

Preferred antimicrobial agents are in bold font.

Postexposure Prophylaxis after *Bacillus anthracis* Exposure in Adults and Children*
Adults
Ciprofloxacin 500 mg PO q 12 h **or** **Doxycycline** 100 mg PO q 12 h **or** Levofloxacin 750 mg PO q 24 h **or** Moxifloxacin 400 mg PO q 24 h **or** Clindamycin 600 mg PO q 8 h **or** Penicillin VK(1) 500 mg PO q 6 h **or** Amoxicillin(1) 1 g PO q 8 h
Children (1 month of age and older)
Ciprofloxacin 30 mg/kg/day PO divided q 12 h (max 500 mg/dose) **or** **Doxycycline** <45 kg: 4.4 mg/kg/day PO divided q 12 h (max 100 mg/dose); >45 kg: 100 mg/dose PO given q 12 h **or** Levofloxacin(2) <50kg: 16 mg/kg/day PO divided q 12 h (max 250 mg/dose); >50 kg: 500 mg PO given q 24 h. **or** Clindamycin 30 mg/kg/day PO divided q 8 h (max 900 mg/dose) **or** **Amoxicillin**(1) 75 mg/kg/day, PO divided q 8 h (max 1 g/dose) **or** Penicillin VK(1) 50-75 mg/kg/day PO divided q 6 to 8 h (1) for penicillin-susceptible strains (2) safety data for levofloxacin use greater than 14 days in the pediatric population is limited
***The PEP antimicrobial regimen should continue for 60 days, combined with three doses of anthrax vaccine (BioThrax). Preferred antimicrobial agents are in bold font.